REMARKS

1. STATUS OF CLAIMS

Claims 60, 61, 64-68, and 70-72 are pending in the application.

Claims 60 and 61 are amended to clarify that the polymer is non-leachably bound to the substrate surface and is not readily washed off. Support for the amendments is found in the Abstract, and paragraphs [0054], [0066], and [0067] of the specification as filed and published (U.S. 2005/0033251).

2. THE OFFICE ACTION OF AUGUST 13, 2008

Rejections

The Examiner, in a Final Office Action mailed August 13, 2008, rejected all of the pending claims in the application.

A. Claim 61 was rejected under 35 U.S.C. § 102(b) as being anticipated by Ward et al. U.S. 5,575,993 ("Ward").

B. Claims 61 and 70-72 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Batich et al. U.S. Appl. 2002/0177828 ("Batich") in view of Ward.

C. Claims 60 and 64-68 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Batich in view of Schoenfeldt et al. U.S. Appl. 2002/0172708 ("Schoenfeldt") and further in view of Voorhees et al. U.S. 2004/0235950 ("Voorhees").

3. REQUEST FOR CONTINUED EXAMINATION

Applicants submit a Request for Continued Examination (RCE) along with this Response. This Response includes amendments to the claims 60 and 61. New arguments to support patentability are also raised in the Response. Submission of an RCE with this Response is intended to expedite entry of the present amendment and the conclusion of this patent examination.

4. ARGUMENTS AGAINST EXAMINER'S REJECTIONS

Applicants respectfully traverse the Examiner's rejections of claims 60, 61, 64-68, and 70-72 and request reconsideration and withdrawal of the rejections based on the claim amendments given above and the following remarks.

A. REJECTION OF CLAIM 61 UNDER 35 U.S.C. § 102(b) AS BEING ANTICIPATED BY WARD.

The Examiner asserts that bonding to a surface can have several meanings as to the type of bonding ranging from weak, for example van der Waals forces, to

strong, for example covalent bonds. The Examiner asserts that even though Ward's polymers are washable off of a bandage, that does not mean that there is an absence of weak intermolecular forces that can be considered a binding between the polyquat and the cellulosic material. Furthermore, the Examiner asserts that Applicants' claim does not exclude weak interactions.

Applicants respectfully traverse the anticipation rejection. Even though Ward discloses applications of ionene polymer solutions to gauze in a bandage to prevent opportunistic cutaneous infections [col 14, ln 64-66], the polymers of Ward are not **non-leachably bound** to the substrate. Ward discloses that the polymers can be washed out using normal washing procedures [col 15, ln 2-4].

Applicants have amended claim 61 to recite that the polymers of the invention are non-leachably bound to the substrate. This clarifies that the polymer is bonded to the substrate in such a way that it is not readily washed off. Applicants define non-leaching to mean that "sections of the polymer of the present invention do not appreciably separate from the material ...under standard uses" [0066]. Furthermore, no less than 0.1 percent of the material separates [0066]. Non-leachable refers to the bond between the polymer chain and the substrate [0067].

Applicants' method requires that the polyquat polymer be non-leachably bound to the substrate. Ward teaches that the ionene polymers have an affinity for surfaces and can "adhere" to those surfaces [col 15, ln 12-18]. However, the "adhered" ionene polymers are not non-leachably bound to the surface as evidenced by Ward's disclosure that the polymers are readily washed out using normal washing procedures [col 15, ln 2-4]. Therefore, Ward does not teach a method wherein the polyionic polymer is non-leachably bound to a substrate as recited by Applicants.

In order to anticipate a claim, the prior art reference must teach every element of the claim [MPEP 2131]. Because Ward does not disclose all of the elements of claim 61 as currently amended, Ward cannot anticipate the claim. Applicants respectfully request the Examiner to withdraw the anticipation rejection of claim 61 and allow the claim.

B. REJECTION OF CLAIMS 61 and 70-72 UNDER 35 U.S.C. § 103(a) AS BEING UNPATENTABLE OVER BATICH IN VIEW OF WARD.

Applicants respectfully traverse the rejection and assert that Batich, in view of Ward, does not make claims 61 and 70-72 obvious to one of ordinary skill in the art.

The Examiner admits that Batich does not disclose ionic association of the actives with the ammonium polymer. The Examiner asserts that Ward was used as a secondary reference to combine with Batich to show that it was already known in the art that anionic antimicrobial compounds could be associated to cationic polymers. The Examiner further asserts that it would have been obvious to one of

ordinary skill in the art that Batich and Ward are combinable. The Examiner concludes that it would be obvious to combine Batich and Ward to obtain Applicants' claimed method of treating a wound which comprises applying a material comprising a substrate which is non-leachably bound to a polyionic polymer which is ionically associated with an anionic antibiotic, analgesic, anti-inflammatory, or a combination thereof.

Claim 61 of the present application recites, among other limitations, that the "polyionic polymer is inherently antimicrobial and is non-leachably bound to said substrate." The claim further recites that "an antibiotic, analgesic, anti-inflammatory, or a combination thereof, [is] ionically associated with said polyionic to achieve extended release of said antibiotic, analgesic, anti-inflammatory, or combination thereof onto and into said wound..." Even though Ward may teach that anionic antimicrobial compounds can be associated to cationic polymers, Ward does not teach or suggest that the cationic polymer be non-leachably bound to a substrate. Ward teaches that incorporation of the bio-active compounds into an ionene polymer increases the solubility of the active material versus the bioactive alone. Thus, the resulting polymer is more prone to be soluble in water and dissolved [col 12, ln 21-34]. Ward also teaches that iodinated ionene polymers impregnated in gauze and textiles are wound cleansing and disinfecting agents. However, those ionene polymers are readily washed from the substrate [col 14, ln 61 to col 15, ln 4]. Ward does not teach or suggest that such antimicrobial compounds associated with the polymer are non-leachably bound to the substrate. Ward effectively teaches away from the concept of having a cationic polymer/anionic active wherein the cationic polymer is non-leachably bound to a substrate. Applicants therefore do not agree that it would be obvious to one skilled in the art to combine Batich with Ward. Furthermore, Under KSR it is legally insufficient to conclude that a claim is obvious just because each feature of a claim can be independently shown in the cited art. (KSR International Co., v. Teleflex Inc. et al, 550 U.S., 398, 127 S.Ct. 1727, 1741).

Batich discloses cationic polymers that are non-leachably bound to substrates. One of ordinary skill in the art would not consider the polymers of Ward which also have enhanced water solubility, as a source of ideas for improving the substances of Batich which would also retain their non-leaching characteristics. As explained above, Ward teaches away from that concept. Rather, Ward teaches the concept of a polymer being readily washed from a substrate.

Furthermore, the Examiner has failed to show that the combination of Batich and Ward cites all the features of Applicants' invention. Even though Batich may show quaternary ammonium polymers similar to Applicants', Ward may show that biologically active anionic species can be "associated" with an ionene polymer, the combination does not suggest that one could obtain a biologically active anionic species associated with a quaternary ammonium polymer which also has the features of non-leachably bonding the polymer to a surface and allowing extended release of the biologically active anionic material.

Applicants further assert that one of ordinary skill in the art would not have

had a reason to combine the teachings of the non-leachably bonded polymers of Batich with the teachings of the readily soluble polymers of Ward because these are opposite concepts. Batich discloses and exemplifies that the bonds of the quaternary ammonium polymer or co-polymer are stable when exposed to body fluids and other aqueous environments [0055]. The polymers readily absorb aqueous solutions [0058] and, when bound to the substrate, are NOT rinsed off with aqueous rinsings [Example 1]. In contrast, Ward discloses solutions of ionene polymers comprising polyquaternary ammonium compounds having anionic biologically-active compounds associated with the compounds. Ward discloses that the solutions of ionene polymers may be applied to gauze. However, the ionene polymers are not non-leachably bound to the gauze and can be readily washed out during normal washings [col 14, ln 61 to col 15, ln 4]. Thus, there is no reason for one of ordinary skill in the art to combine the opposite concepts related to water solubility taught in Ward and Batich.

Applicants assert that the combination of Batich with Ward does not make obvious to one of ordinary skill in the art the invention as claimed in claims 61 and 70-72 of the instant application. Batich does not suggest combining anionic therapeutic agents with quaternary ammonium polymers to achieve extended release characteristics. Neither does Ward supply what is missing from the disclosure of Batich as discussed above with regard to claim 61.

Applicants respectfully request the Examiner to withdraw the obviousness rejection of claims 61 and 70-72 and allow the claims as currently amended.

C. REJECTION OF CLAIMS 60 and 64-68 UNDER 35 U.S.C. § 103(a) AS BEING UNPATENTABLE OVER BATICH IN VIEW OF SCHOENFELDT AND VOORHEES.

Applicants respectfully traverse the rejection and submit that Batich, in view of Schoenfeldt and Voorhees, does not make claims 60 and 64-68 obvious to one of ordinary skill in the art.

The Examiner asserts that Batich discloses Applicants' invention except that it does not disclose ionic association of the actives with the ammonium polymer. Further Batich does not disclose the use of the matrix metalloproteinase (MMP) inhibitors, ilomastat or GM1489. Schoenfeldt was used as secondary reference to show that it was already known in the art that ilomastat could be associated to cationic polymers. Voorhees was used for its disclosures of ilomastat and GM1489 as MMPIs. The Examiner concludes that it would be obvious to combine Batich, Schoenfeldt, and Voorhees to obtain Applicants' claimed method of treating skin ulcers, bed sores, or chronic wounds with a material comprising a substrate and a non-leachably bound quaternary ammonium polymer or copolymer wherein said polymer or copolymer is ionically associated with and achieves extended release of an MMPI such as ilomastat, GM1489, or C-terminal form of ilomastat.

Applicants incorporate by reference and reassert their arguments concerning Batich, Schoenfeldt, and Voorhees presented in the June 3, 2008 Response and the

Remarks concerning Batich above in Section B. In summary, Batich does not teach or suggest a matrix metalloproteinase inhibitor, which is ionically associated with a quaternary ammonium polymer or copolymer wherein said polymer or copolymer is non-leachably bound to a substrate to achieve extended release of said matrix metalloproteinase inhibitor as recited in claim 60.

Batich discloses that the cationic antimicrobial groups, the quaternary ammonium groups, may be intentionally made to be more susceptible to release [0057]. However, there is no disclosure or suggestion in Batich that **anionic** antibiotic, analgesic, or anti-inflammatory substances be associated with the cationic groups. Furthermore, there is no disclosure or suggestion in Batich that matrix metalloproteinase inhibitors would have extended release characteristics when associated with the polyionic polymers.

Schoenfeldt discloses a method of preparing a sol gel comprising crosslinked polyionic polymers and pharmaceutical medicaments. The sol gel is dehydrated to provide a non-fibrous porous material which may be used as a preparation for a dressing or an absorbent article [0016]. The material is swellable but is not soluble in water [0056]. Schoenfeldt discloses that active ingredients may be incorporated into the sol gel but is silent regarding whether the actives have extended release properties.

Schoenfeldt does not suggest quaternary ammonium polymers or copolymers being components of polyionic polymers as recited in Applicants' claim 60. Schoenfeldt also does not suggest that the sol gel be non-leachably bound to a substrate.

Schoenfeldt discloses that primary, secondary, or tertiary amines are cationic groups that can be linked to a cationic polymer [0041]. The amines may be protonated with sulphates, acids, etc. to give the corresponding primary, secondary, and tertiary ammonium salts. Schoenfeldt discloses that primary amines are preferred cationic groups attached to the polymer backbone [0042]. Applicants assert that Schoenfeldt's disclosure implies that primary ammonium salts would be preferred over secondary or tertiary ammonium salts. Schoenfeldt does not disclose the use of quaternary ammonium salts. After reading Schoenfeldt, one of ordinary skill in the art would not be encouraged to try a secondary, tertiary, or a quaternary ammonium salt. Schoenfeldt teaches that primary ammoniums are preferred [0042]. Hence ammoniums having alkyl on the amine functionality are not preferred. A quaternary amine consists of four alkyl or aryl groups attached to an N (nitrogen) atom. [Considine, Douglas M., editor "Van Nostrand's Scientific Encyclopedia 5th Ed.", "Amines", page 113, Van Nostrand Reinhold, Co., publishers (1976)]. Therefore, taken to the extreme four alkyl groups would be even less preferred by Schoenfeldt. Applicants assert that based on Schoenfeldt's disclosure [0040, 0041, 0042], one of ordinary skill in the art would not have expected that substituting quaternary ammonium polymers in place of the primary ammonium polymers of Schoenfeldt would produce useful polymers. Schoenfeldt's disclosure is a teaching away from the use of quaternary ammonium groups because Schoenfeldt both prefers primary ammonium and does not disclose the use of quaternary

ammonium.

Voorhees discloses treatments for acne by topical, systemic (preferably oral), or a combination thereof applications of compositions comprising an effective amount of a non-retinoid or non-glucocorticoid inhibitor [0010]. The inhibitor may be a combination of an MMP inhibitor and an elastase inhibitor [claim 17]. Voorhees includes a long list of references to possible elastase inhibitors including trialkylammonium salts and alkyltrimethylammonium salts. [0044].

Voorhees does not disclose or suggest the use of **polymeric** ammonium salts. Voorhees does not disclose or suggest that the ammonium salts have any effect on the release of the other components of the mixture, including the MMP inhibitors, when applied to the skin or taken orally. Voorhees does not disclose or suggest that the compositions are non-hydrolyzably bound to a substrate nor are the compositions discloses or suggested to be absorbent materials.

Batich alone does not anticipate or make obvious to one of ordinary skill in the art Applicants' invention as claimed in any one of claims 60 and 64-68. One of ordinary skill in the art would not look to Schoenfeldt and Voorhees to supply what is missing from the disclosure of Batich with regard to claim 60. Schoenfeldt teaches away from the use of quaternary ammonium compounds. Voorhees does not disclose methods of binding the ammonium salts to a substrate nor does Voorhees disclose methods of using the compositions in conjunction with an insoluble substrate. Neither Schoenfeldt nor Voorhees suggests binding their compositions to a substrate that is a woven or nonwoven, solid, or flexible mass in order to obtain extended release of bioactive components as disclosed by Applicants.

The concept of extended release of anionic actives is not disclosed or taught in Batich, Schoenfeldt, or Voorhees. Therefore, Applicants assert that it is not possible for one of ordinary skill in the art to have obtained any reason from the cited references to develop Applicants' claimed invention with respect to extended release of the MMPI bioactive materials.

The Examiner asserts that Schoenfeldt teaches the use of combinations of polycationic polymers with amine groups and ilomastat. The Examiner concludes that the ionic interaction between the active and the polyionic polymer claimed by Applicants would be an inherent characteristic of the combinations Schoenfeldt teaches. Applicants respectfully disagree. The inherency and obviousness of a characteristic are distinct questions. "That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." *In re* Spormann, 363 F.2d 444, 448, 150 USPQ 449, 452 (C.C.P.A. 1966). Applicants assert that it is improper for the Examiner to raise the issue of inherency in an obviousness rejection.

Therefore, Applicants assert that the combination of Batich, Schoenfeldt, and Voorhees does not make obvious the invention as claimed. Applicants respectfully request the Examiner to withdraw the obviousness rejection of claims 60 and 64-68 and allow the claims as currently amended.

5. OTHER MATTERS

Applicants submitted an Information Disclosure Statement (IDS) with their Response of November 6, 2006 which included an erroneous citation. Cite No. 4 under Non-Patent Literature (page 3) incorrectly lists the page numbers for the ONABE reference. The cite should be corrected as follows:

"Journal of Applied Polymer Science, Vol. 22, ~~2495~~ 3495-3510 (1978) John Wiley & Sons, Inc."

The correct pages of the reference were submitted to the Examiner and the Examiner reviewed the reference December 15, 2006. We are submitting the enclosed replacement sheet to correct the typographical error printed on the IDS form. Submitted herewith is a Replacement Sheet for page 3 of the November 6, 2006 IDS submitted by Applicants in support of the present application.

CONCLUSION

Applicants respectfully traverse all of the rejections. Claims 60 and 61 are amended to further distinguish them from the prior art. The amended claims are not anticipated because the prior art does not disclose each and every element of the claims. Claims 60 and 64-68 are not made obvious to one of ordinary skill in the art by the disclosures of Batich, Schoenfeldt, and Voorhees as described above. Claims 61 and 70-72 are not made obvious to one of ordinary skill in the art by the disclosures of Batich, and Ward as described above.

For the foregoing reasons, Applicants submit that the claims presented herewith are patentable over the prior art of record and respectfully solicits prompt action thereon. If any questions remain, the Examiner is invited to phone the undersigned attorneys.

Respectfully submitted: December 12, 2008

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